Relationship between HDL-Cholesterol and Angiographic Severity of Coronary Artery Disease

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Abstract:
Background: Dyslipidaemias is one of the major risk factor for Coronary artery diseases (CAD). There is an inverse correlation between high density lipoprotein cholesterol (HDL-C) and the risk of coronary artery disease. Understanding the angiographic characteristics of coronary artery diseases (CAD) in low and normal HDL-C patients and its association with severity of CAD is very important for future intervention. Although high-density lipoprotein cholesterol (HDL-C) is well established predictor of future cardiovascular event, little information is available regarding its correlation with the prevalence and severity of angiographically evaluated coronary artery diseases (CAD).

Materials and Methods: This cross-sectional comparative study was conducted in the Department of Cardiology, Sylhet MAG Osmani Medical College Hospital, Sylhet during the period from January 2012 to December 2013. We included 100 patients with coronary artery diseases and divided into two groups. 50 patients with low HDL-C (<40 mg/dl) were taken in study group (Group-A) and 50 patients with normal HDL-C (>40 mg/dl) were taken in control group (Group-B) according to inclusion and exclusion criteria. Coronary angiography was performed via the trans-femoral approach using standard techniques. Severity of CAD was determined by vessels score and Friesinger score.

Results: The age [51.1 (SD 8.7) years vs 51.4 (SD 8.2) years; p>0.05] and sex [45 (90.0%) male and 5 (10.0%) female vs 41 (82.0%) male and 9 (18.0%) female; p=0.249] were similar in group-A and group-B. The conventional risk did not show any significant difference between low and normal HDL level group such as age, sex, smoking, diabetes mellitus, hypertension, BMI, hypercholesterolaemia, high serum LDL, hypertriglyceridaemia and family history of CAD (p>0.05 each).

No significant vessel disease [3 (6.0%) vs 14 (28.0%); p=0.008] and single vessel disease [11 (22.0%) vs 25 (50.0%); p=0.020] were significantly fewer in group A than that of group-B; while double vessel disease [14 (28.0%) vs 5 (10.0%); p=0.039] and triple vessels disease [22 (44.0%) vs 6 (12.0%); p=0.002] were significantly higher in group-A than that of group-B. Friesinger score 0 [3 (6.0%) vs 11 (22.0%); p=0.033] and Friesinger score 1 to 4 [6 (12.0%) vs 24 (48.0%); p=0.01] were significantly fewer in group A than that of group-B; while Friesinger score 5 to 9 [20(40.0%) vs 9 (18.0%); p=0.041] and Friesinger score 10 to 15 [21 (42.0%) vs 6 (12.0%); p<0.004] were significantly higher in group-A than that of group-B. Among all respondents conventional risk factors were not statically significant between the groups. A significant negative correlation was found between serum HDL-C (mg/dl) and number of diseased vessel (r=0.370; p<0.001) and also Friesinger score (r=0.388; p<0.001).

Conclusion: It may be concluded that low HDL-C level is associated with angiographically more severe coronary artery diseases reflected by vessels score and Friesinger score as compared to normal or high HDL-C level.

Key words: Coronary artery diseases, HDL, Lipoprotein angiography

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Introduction:
Cardiovascular disease is one of the leading causes of morbidity and mortality in the world. It is responsible for about 30% of deaths worldwide. By 2020, it is predicted that coronary artery disease will claim 25 million lives annually and that coronary artery disease (CAD) will surpass infectious disease as the world’s number one cause of death and disability. The South Asian countries of India, Pakistan, Bangladesh, Sri-Lanka, and Nepal contribute the highest proportion of the burden of cardiovascular diseases (CVDs) compared to any other region globally. Estimates from the Global burden of Disease Study suggests that by the year 2020 this part of the world will have more individuals with atherosclerotic cardiovascular disease than any other region.

Deaths related to CVD also occurs 5 to 10 years’ earlier in South Asian countries than they do in Western countries. This has raised the possibility that South Asians exhibit a special susceptibility for coronary artery disease that is not explained by traditional risk factors. Factors such as age, family history, abnormal blood lipid profile, hypertension, diabetes mellitus and smoking have been shown to be effective on coronary artery disease incidence. Although such factors are also thought to determine the severity and extent of coronary atherosclerosis.

Dyslipidemias, including high low-density lipoprotein cholesterol (LDL-C) and triglyceride (TG) concentrations and low high-density lipoprotein cholesterol (HDL-C) concentration, are risk factors for CHD. One of the major predisposing factors to atherosclerosis is an abnormal lipoprotein metabolism and it may be present in over 70% of patients with premature CAD.

Low-density lipoprotein (LDL) seems to be the major target of oxidative modification, making it particularly atherogenic. Identification of factors protecting against oxidative modification of LDL are therefore of major interest. High-density lipoprotein (HDL) has been shown to have antioxidative potential; however, the mechanism(s) of its action is not known. One mechanism might be the enzymatic removal of lipid peroxides accumulating on the LDL particle by enzymes present on HDL. Thus high concentration of LDL cholesterol and low levels of HDL cholesterol are able to promote atheroma formation and are recognized as particularly important risk factors for atherosclerosis and CAD.

Persons with low HDL cholesterol levels are at increased risk of coronary heart disease, restenosis after angioplasty, and death from cardiovascular causes, especially if such persons are male or have diabetes. In addition, angiographic studies have shown a correlation between low HDL cholesterol levels and increased number of diseased coronary arteries. Low HDL C values were associated with an increased both triple vessel disease and left main coronary artery. One study found a fourfold increase in the rate of restenosis after angioplasty in patients with low HDL cholesterol levels.

Severity of CAD is inversely correlated with levels of HDL-C in both men and women. In multivariate analysis HDL-C is inversely related to the mean percentage increase in coronary artery stenosis than other lipid.

In angiographic studies the relation between HDL-C levels and CAD has varied widely ranging from significant inverse correlation with HDL-C and were the only significant predictor of the number of lesions.

Materials and method:
This cross-sectional comparative study was conducted in department of cardiology, MAG Osmani Medical College and hospital, Sylhet, Bangladesh during the period from 1st January 2012 to 31st December 2013 to explore the association of low HDL-cholesterol with angiographic severity of coronary artery diseases of patient include chronic stable angina (CSA) and acute coronary syndrome (ACS). Considering the inclusion criteria like patient with coronary artery diseases irrespective of age and sex and exclusion criteria like prior coronary revascularization either CABG or angioplasty, congenital heart diseases, valvular heart diseases, cardiomyopathy, renal insufficiency, LDL-C more than 130 mg/dl, patient refuses to undergo CAG or enroll in the study. 100 patient getting guideline directed anti lipid therapy after initial diagnosis of coronary artery diseases and treated conservatively who subsequently underwent coronary angiogram were included in this study by purposive sampling. Fasting lipid profile was measured following a 12 hour fast and serum total cholesterol (TC), triglyceride (TG) and high density lipoprotein (HDL-C) were determined by standard method using CX 7 SYNCHRON clinical system. LDL cholesterol (LDL-C) was calculated using the Friedewald equation. 50 patient were in Group-A with low HDL-C and 50 patient were in Group-B with normal HDL-C level within index hospital admission, the enrolled patient underwent coronary angiography (CAG) and was analysed by visual estimation and severity was assessed by vessels score and Friesinger score.

Vessel score is the number of vessels with a significant stenosis (for left main coronary artery 50% or greater and for others 70% or greater reduction in luminal diameter). Score ranges from 0 to 3, depending on the number of vessel involve. Left main coronary artery was scored as single vessel disease.
Score 0 = no vessel involvement.
Score 1 = single vessel involvement.
Score 2 = double vessel involvement.
Score 3 = triple vessel involvement.

The Friesinger score,\(^1\) ranges from 0 to 15. Each of the three main coronary arteries is scored separately from 0 to 5.

Score 0: No arteriographic abnormality
Score 1: Trivial irregularities (lesion from 1-29%)
Score 2: Localized 30-68% luminal narrowing
Score 3: Multiple 30-68% luminal narrowing of same vessel;
Score 4: 69-100% luminal narrowing without 100% occlusion of proximal segments
Score 5: Total obstruction of a proximal segment of a vessel.

**Statistical Analysis:**

Data were processed and analyzed with the help of computer program SPSS (Statistical package for social sciences) 16 version. Quantitative data were analyzed by mean and standard deviation; and comparison was done between two groups by Z-test. Qualitative data was analyzed by rate, ratio, and percentage; and comparison was done between two groups by Chi-Square test. A probability (p) value of <0.05 was considered statistically significant.

**Result:**

Mean age was found 50.1±8.7 and 51.4±8.2 years in group–A and group-B respectively (p>0.05) in both group maximum patient age belongs to 41-50 years. Male were predominant in both groups, 45(90%) in group-A and 41(82%) in group-B. Risk factor including smoking, HTN, DM and obesity was 26(52%) vs. 29(58%), 29(58%) vs. 26(52%), 19(38%) vs. 23(46%) and 22(44%) vs. 19(38%) in group-A and group-B respectively and regression analysis shows there was no statistically significant difference among the other variables. Fasting blood sugar, serum creatinine and serum HDL-C was found 141.82±37.9 vs. 140.42±38.37 mg/dl, 1.18±0.13 vs. 1.21±0.16 mg/dl and 33.86±3.39 vs. 46.96±4.96 mg/dl in group-A and group-B respectively. HDL-C difference was found statistically significant between two group (table I).

Regarding coronary artery involvement vessel score 0 and vessel score 1 was 3(14%) vs. 14(28%) and 24(48.0%) vs. 11(22%) in group-A and group-B respectively which was statistically significant (p<0.05). On the other hand vessel score 2 and vessel score 3 was 6(12%) vs. 4(8%) in group-A and group-B respectively which is statistically significant. Left main coronary artery involvement 6(12%) vs. 4(8%) in group-A and group-B respectively was not statistically significant (table III).

Friesinger score 0 [3 (6.0%) vs 11 (22.0%) p=0.033] and Friesinger score 1 to 4 [6 (12.0%) vs 24 (48.0%) p=0.01] were significantly fewer in group A than that of group B; while Friesinger score 5 to 9 [20(40.0%) vs 9 (18.0%) p=0.041] and Friesinger score 10 to 15 [21 (42.0%) vs 6 (12.0%) p<0.004] were significantly higher in group-A than that of group-B (table-III).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group A(n=50)</th>
<th>Group B(n=50)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>50.1±8.7</td>
<td>51.4±8.2</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>FBS (mg/dl)</td>
<td>141.82±37.99</td>
<td>140.42±38.37</td>
<td>p = 0.855</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>1.18±0.13</td>
<td>1.21±0.16</td>
<td>p = 0.217</td>
</tr>
<tr>
<td>Serum Cholesterol</td>
<td>186.94±31.03</td>
<td>196.14±25.13</td>
<td>p = 0.107</td>
</tr>
<tr>
<td>Serum HDL</td>
<td>33.86±3.39</td>
<td>45.96±4.96</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Serum LDL</td>
<td>113.64±23.16</td>
<td>107.86±25.12</td>
<td>p = 0.235</td>
</tr>
<tr>
<td>Serum TG</td>
<td>177.28±60.20</td>
<td>164.78±24.85</td>
<td>p = 0.118</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Variables</th>
<th>n</th>
<th>%</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>45</td>
<td>90</td>
<td>41</td>
<td>82</td>
</tr>
<tr>
<td>Female</td>
<td>5</td>
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<td>9</td>
<td>18</td>
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<tr>
<td>Smoking</td>
<td>26</td>
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<td>29</td>
<td>58</td>
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<td>DM</td>
<td>19</td>
<td>38</td>
<td>23</td>
<td>46</td>
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<tr>
<td>HTN</td>
<td>29</td>
<td>58</td>
<td>26</td>
<td>52</td>
</tr>
<tr>
<td>F/H of IHD</td>
<td>12</td>
<td>24</td>
<td>7</td>
<td>14</td>
</tr>
<tr>
<td>Obesity</td>
<td>24</td>
<td>44</td>
<td>19</td>
<td>38</td>
</tr>
</tbody>
</table>
**Discussion:**

Age of the patients ranged from 30 to 70 years with the mean age of 50.8 (SD 8.5) years. The mean age of the patients of Group-A and Group-B were almost similar [50.1 (SD 8.7) years vs 51.4 (SD 8.2) years; p>0.05). This result was consistent with the study of Zaher et al. that the mean age of their patients with coronary artery disease was 49.85 ± 9.89 years. This result was also correlated with the study of Arnesen et al. that the mean age of the patients with coronary artery disease was 51.3 ± 7.3 years.

This result also demonstrated that 41 (41.0%) patients were in the age group of 41 to 50 years, 34 (34.0%) patients were in the age group of 51 to 60 years, 13 (13.0%) patients were in the age group up to 40 years and 12 (12.0%) patients were in the age group of above 60 years. Similar result was reported in the study of Shirin et al. that 80.0% of their series were male and 20.0% of patients were female.

In the current study 55.0% of patients were smoker and 45.0% of patients were non-smoker. There was no significant difference of smoking status between low HDL-C group and normal HDL-C group (p=0.546). This result was correlated with the study of Kabir et al. that 60.0% of their patients of CAD were smoker.

Among the total 100 patients in the present study, 42.0% of patients were diabetic and 58.0% of patients were non-diabetics. There was no significant difference of diabetes mellitus between the groups (p=0.418). This result was correlated with the study of Bertoluci et al. that 48.6% of their CAD patients were diabetic.

Among the total 100 patients in this study, 55.0% of patients were hypertensive and 45.0% of patients were

<table>
<thead>
<tr>
<th>Table-II</th>
<th>Distribution by type of coronary artery disease (n=100)</th>
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<tbody>
<tr>
<td></td>
<td>Group A (n=50)</td>
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<tr>
<td>Type of CAD</td>
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<tr>
<td>Chronic stable angina</td>
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<tr>
<td>Unstable angina</td>
<td>20</td>
</tr>
<tr>
<td>NSTEMI</td>
<td>7</td>
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<td>STEMI</td>
<td>17</td>
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<table>
<thead>
<tr>
<th>Table-III</th>
<th>Comparison of coronary angiographic severity between two groups (n=100)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Group A (n=50)</td>
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<tr>
<td>Vessel score</td>
<td>n</td>
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<tr>
<td>No involvement</td>
<td>3</td>
</tr>
<tr>
<td>Single vessel</td>
<td>11</td>
</tr>
<tr>
<td>Double vessel</td>
<td>14</td>
</tr>
<tr>
<td>Triple vessel</td>
<td>22</td>
</tr>
<tr>
<td>LMCA</td>
<td>6</td>
</tr>
<tr>
<td>Friesinger Score</td>
<td>0 (Normal)</td>
</tr>
<tr>
<td>1-4 (Mild)</td>
<td>6</td>
</tr>
<tr>
<td>5-10 (Moderate)</td>
<td>20</td>
</tr>
<tr>
<td>11-15 (Severe)</td>
<td>21</td>
</tr>
</tbody>
</table>

Relationship between HDL-Cholesterol and Angiographic Severity
Mohammed Iqbal Ahmed et al.  
Bangladesh heart j Vol. 33, No. 1  
January 2018
normotensive. This result was similar to the study of Habib et al.\textsuperscript{29} found that the prevalence of hypertension was 54.9% of their CAD patients. This result was also supported by Okamatsu et al.\textsuperscript{30} that 54.0% of their patients were hypertensive. In this regards Asakura et al.\textsuperscript{28} found 60.0% of their patient were hypertensive.

Among the total 100 patients in the current study, 19.0% of patients had family history of CAD and 81.0% of patients had no family history of CAD. There was no significant difference of family history of CAD between group-A and group-B (p=0.202). Khadem-Ansari et al.\textsuperscript{20} reported that the history of familial CHD was 27.3% of their CAD patients. Senaratne et al.\textsuperscript{32} found 28.2% of their South Asian patients had family history.

Among the total 100 patients in the present study, type of CAD was unstable angina in 35 (35.0%), ST-elevation MI in 33 (33.0%), non-ST-elevation myocardial infarction (MI) in 20 (20.0%) and chronic stable angina in 12 (12.0%) patients. No significant difference was found between Group-A and Group-B in terms of type of CAD (p=0.467). This result was supported by the study of Kabir et al.\textsuperscript{27} that stable angina in 18% unstable angina in 36% and MI in 46% of their series of CAD patients.

In this series no significant vessel involvement was in 17.0%, single vessel disease in 36.0%, double vessel disease in 19.0% and triple vessel disease in 28.0% of cases. Kazemi et al.\textsuperscript{33} reported that single vessel disease in 22.3%, double vessel disease in 21.8% and triple vessel disease in 23.4% and no vessel disease in 32.5% of their patients underwent coronary angiogram.

No vessel disease and single vessel disease were significantly fewer in group A than that of group-B; while double vessel disease and triple vessels disease were significantly higher in group-A than that of group-B. Safeer and Cornell,\textsuperscript{16} found that low HDL cholesterol levels was associated with increased number of diseased coronary arteries and increased incidence of triple vessel disease. Drexel et al.\textsuperscript{34} found that 21.8% single vessel disease, 26.5% double vessel disease and 51.7%- triple vessel disease in low HDL-C level in patients with CAD. Friesinger score 0 [3 (6.0%) vs 11 (22.0%); p=0.033] and Friesinger score 1 to 4 [6 (12.0%) vs 24 (48.0%); p=0.01] were significantly fewer in group A than that of group-B; while Friesinger score 5 to 9 [20(40.0%) vs 9 (18.0%); p=0.041] and Friesinger score 10 to 15 [21 (42.0%) vs 6 (12.0%); p<0.004] were significantly higher in group-A than that of group-B. In this regards French et al.\textsuperscript{35} found that more significant coronary artery lesions associated with low HDL-C patients (77.0%). Ballantyne et al.\textsuperscript{36} found that percentage of diameter stenosis was more in low HDL-C patients. Rahman et al.\textsuperscript{37} found low HDL-C associated with large lesions.

In the present study there was a significant negative correlation between serum HDL (mg/dl) and number of disease vessel (p<0.001). This result was consistent with the study of Tarchalski et al.\textsuperscript{12} that there was inverse association between HDL-C level and the number of diseased coronary vessel.

The conventional risk factors were statistically similar in low and normal HDL level group smoker, diabetes mellitus, hypertension, hypercholesterolaemia, high serum LDL, hypertriglyceridaemia and family history of CAD in both multivariate analysis. This results were some different from the study of Zaher et al.\textsuperscript{22} These may be due to selection criteria and difference in the study group selection. Zaher et al.\textsuperscript{22} selected patients with CAD as case and without CAD as control. But in the present study both groups were patients with CAD and difference in HDL-C level between group i.e CAD with low HDL-C in study group and CAD with normal HDL-C in control group.

**Conclusion:**

From the findings of the present study it may be concluded that low HDL-C level is associated with angiographically more severe coronary artery diseases in comparison to normal or high HDL-C patients reflected by vessels score and friesinger score.

**References:**


